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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,583	02/14/2000	KOICHI ENDO	ENDO=12	5957

7590 11/05/2003

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WASHINGTON, DC 20001

EXAMINER

YU, GINA C

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 11/05/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,583

Applicant(s)

ENDO ET AL.

Examiner

Gina C. Yu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9,12-16 and 19-26 is/are pending in the application.
- 4a) Of the above claim(s) 12-14 and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8,9,15,16 and 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt is acknowledged of Amendment filed on August 11, 2003. Claim rejections made under 35 U.S.C. § 112, second paragraph as indicated in the Office action dated April 7, 2003 are modified to meet the amended claims. Claim rejections made under 35 U.S.C. § 103 (a) are also modified to meet the claim amendments. The substance of the rejections are maintained otherwise.

Claims 8, 9, 12-16, and 19-26 are pending, of which claims 12-14 and 19-21 have been withdrawn from consideration. Claims 8, 9, 15, 16, 22-26 are examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, 25, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "kit" renders the claims vague and indefinite, as it is not clear as to what type or form of kit applicants are claiming. The term is not defined in the applicants' disclosure, nor it is readily apparent to a one having ordinary skill in the art. Examiner views that the newly inserted term "as a bone mass-maintenance drug to maintain bone mass in a pharmaceutically acceptable carrier" does not structurally define the components of the "kit".

The term "instruction" also renders the claims vague and indefinite, as there is no explanation as to how the "kit" is to be used.

The remaining claims are rejected as depending on indefinite base claim.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 8, 9, 15, 16, 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Pharmacological Basis of Therapeutics (1996) ("Therapeutics") in view of Hukkanen et al. (Endocrinology) and Moore et al. (J. of Med.).

Therapeutics teaches the method of treating osteoporosis by administering estrogen, thereby inhibiting the activity of IL-6 (p. 1541, col. 1, last paragraph). Examiner takes the position that the newly added phrase "as a bone mass-maintenance drug to maintain bone mass in a pharmaceutically acceptable carrier" is a preamble which recites intended use or the purpose of using IL-6 inhibitors to treat osteoporosis. See MPEP 2111.02.

The reference fails to teach a kit comprising L-N-6-(1-iminoethyl)lysine, the elected species, nor does it teach a method of using the same to treat osteoporosis.

Hukkanen et al. teach that iNOS inhibitors completely inhibit the activity of cytokines such as IL-6. See p. 5452, col. 1, bottom of 1st full paragraph.

Moore et al. teach that L-N-6-(1-iminoethyl)lysine is a potent and selective iNOS inhibitor. See p. 3886, abstract. While Moore et al. does not disclose whether the elected iNOS inhibitor, L-N-6-(1-iminoethyl)lysine, meets the recited requirement in

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instant claims, examiner takes the position that the limitation is an inherent property in the inhibitor itself.

Given the general teachings of Therapeutics that osteoporosis can be treated by inhibiting the activity of IL-6, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the prior arts such as Hukkanen for specific IL-6 inhibitors such as iNOS inhibitors. The skilled artisan would have been further motivated to use L-N-6(1-iminoethyl)lysine, as motivated by Moore et al., because of the expectation that administering the potent and selective iNOS would successfully treat osteoporosis.

Response to Arguments

Applicant's arguments filed on August 11, 2003 have been fully considered but they are not persuasive.

Applicants argue that the teaching of the Hukkanen reference is limited to the relationship of NOS inhibitors and IL-1 β . Examiner respectfully disagrees. As indicated in the previous Office action, the Hukkanen reference teaches that iNOS inhibitors completely inhibit the activity of cytokines such as IL-6. See p. 5452, col. 1, bottom of 1st full paragraph. Examiner notes that it is well known in patent law that in considering the disclosure of a reference, "it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom". See In re Preda, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). See also MPEP § 2144.01.

While applicants assert that each of Therapeutics, Hukkanen, and Moore lacks the complete aspect of the claimed invention, there is no arguments provided to rebut the motivation to combine the references as indicated in the obviousness rejection. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants arguments that the references submitted on January 14, 2003 indicates that a skilled artisan would not have been motivated to use the selective iNOS inhibitors, examiner notes that the currently cited the references were also available prior arts to a skilled artisan at the time of the present invention, and the alleged nonobviousness of the invention should be shown in view of those combined prior arts.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gina C. Yu whose telephone number is 703-308-3951.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 703-305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Gina C. Yu
Patent Examiner
November 1, 2003



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

11/3/03